

Bigelow (J. M.)

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* **SVAPNIA,**

OR PURIFIED OPIUM,

Consisting of Meconates of Morphia, Codeia and Narceia, and made by assay. An important substitute for Morphia and Crude Opium.

BY DR. J. M. BIGELOW, DETROIT.

THE tendency of the age is to extreme analysis, and from a purely scientific standpoint, it is probably better that it is so, especially in experiments with such highly compound drugs as opium. It is in this way that modern experimenters have pretty accurately determined the peculiar physiological and therapeutical properties and effects of the six active alkaloids of this most ancient drug; but in a practical point of view, may we not carry this process to extremes? This is acknowledged to be frequently done in the analysis of the various alkaloids of the cinchona plant.

Through the labors of M. Claude Bernard, one of the leading scientists of the present time, M. Ozonane and M. Pelletier, of Europe, and Dr. Squibb and Dr. DaCosta, of this country, many of the problems with regard to the peculiar effects of the alkaloids of opium have been successfully wrought out by critically analyzing, observing and experimenting on animals and in clinical practice; thus the effects of each one of these active alkaloids have been studied and developed in detail.

They place narceine, morphine and codeine almost exclusively in the list of soporifics, anodynes and calmatives. Dr. DaCosta, however, does not confirm the opinion of the European physiologists that narceine holds the first place as a soporific.

Morphine acts principally upon the brain; codeine especially on the cerebellum, medulla oblongata and pneumogastric nerves. When one grain of morphine was injected into one dog, and one

* This article on Svapnia is copied from the January number of the *Detroit Review of Medicine and Pharmacy*.

grain of codeine into another, both slept calmly for three or four hours. Then the morphine dog waked up wildly, recognized no one, looked haggard, and did not recover his good humor till the next day. The codeine dog waked up bright and playful. The experiment was then reversed, each dog being injected with the other's medicine, with exactly the same results. Morphine produces headache and vomiting very soon and before a dangerous dose is arrived at, while codeine does not produce these unpleasant effects, and hence requires more care in its exhibition than morphine when given alone. A large amount of clinical experience has been had with both these principles, but little has been published with regard to codeine, while the therapeutical action of morphine is so well and universally known that little need be repeated here.

Narceine, according to M. Ozonane, exerts a special action on the lumbar portion of the spinal cord, and hence he has frequently given it to paralytic patients subject to severe attacks of pain in the back and loins. Of all the alkaloids of opium, he thinks this is the only one that gives relief in such cases, and it has never disappointed him. His theory is that the painful crisis disappears, and the paralysis diminishes, because the narceine prevents and removes the liability to repeated attacks of congestion. On the other hand, codeine is supposed to act specifically on the medulla oblongata, near the origin of the pneumogastric nerve, on account of its wonderful efficacy in many cases of cough and gastralgia.

In the experience of Dr. DaCosta, although an active agent, narceine does not possess the hypnotic powers ascribed to it by European experimenters.

Dr. Eulenberg (*American Journal of Pharmacy*, May, 1867, from *Repertoire de Pharmacie*) thus writes of the effects of narceine: The repeated internal use often produces from one to two stools, and sometimes even diarrhœa, and for sedative and hypnotic effects is preferable to every other substance. Besides its employment in some essentially neuralgic affections, its use is indicated in all cases where pain is a prominent symptom, as in articular affections, phlegmons, iritis, orchitis, blennorrhœa, epididymitis, cystitis, cirrhosis of the liver, and in wounds or after

painful operations; in all these cases narceine, when employed either internally or externally, in doses of from one-eighth to one-half a grain, rapidly lessens the pain, and often produces a sleep of four, five, or even nine hours—sleep which is soft, tranquil, uninterrupted, and followed by a quiet awakening. These doses never give rise to any derangements or any poisonous effects. Although by the use of morphine, in numerous cases we obtain the same effects, it often fails. Many diseases (especially among women) present, in fact, a kind of idiosyncrasy which renders the employment of morphia impossible; thus, by its internal use, vomiting is produced, or else the medicine causes, instead of refreshing sleep, a state of great excitement, with distressing dreams, delirium and convulsions, while in some other diseases morphine, without appreciable cause, produces only a slight effect, or one of only short duration. Narceine as an anodyne and narcotic, may be always employed in place of morphia, and is, in every respect, equal to it in value, and even in a great many cases is to be preferred to it.

According to Prof. Proctor, the extravagant price of narceine is likely to prevent its use in general practice, the solutions from which morphine has been extracted, containing this alkaloid, having been thrown away. Its solubility varies much from that of morphia, and its reaction to acids is quite different. In SVAPNIA all the narceine of the opium is retained, but the attempt to isolate it from the codeine and morphine produces a decomposition that cannot be artificially rearranged without much expense, and a consequent loss of anodyne and hypnotic power. Hence the peculiar adaptability of this new preparation to all the cases where the calmative alkaloids are applicable. With regard to the proportion of narceine in opium, there is much conflict of opinion, and the numerous analyses thus far made have little tendency to reconcile them. Thus, according to Mulder's analysis, Smyrna opium contains six to thirteen per cent, while Schindler makes it less than three-fourths of one per cent. Dr. Flukeger even goes so far as to estimate all the alkaloids of pseudo-morphine, codeine, thebaine, papaverine, rhœdeine, narceine, kryptopeine and opianine at not much more than one per cent. Mulder's analysis

was probably very wide of the mark, and this fact also explains the wide discrepancy of opinion as to the physiological and therapeutical effects of narceine among physicians of high repute.

The alkaloids narcotine, thebaine and opianine (or papaverine), being eliminated from this preparation, SVAPNIA, do not require at our hands an analysis of their properties. But in passing, we may remark that experiments prove thebaine to be one of the most poisonous principles of opium. One decigramme injected into the veins of a large dog, killed it in five minutes, while it required two grammes, or thirty grains, of morphine to produce a similar effect.

M. Orfila and M. Majer. lie found it to cause tetanus and violent convulsions in the upper limbs, while the legs were scarcely agitated; hence it is supposed that its action is spent on the cervico-dorsal portion of the spinal cord. M. Ozonane found from three to six centigrammes, given to a paralytic patient, produce such agitation and sleeplessness, general uneasiness and excitement, especially of the neck and arms, that it had to be discontinued.

Besides its tetanic and convulsive properties, so distinctively marked, its effects are decidedly the reverse of those of morphine, codeine and narceine.

From these experiments we may very rationally draw the inference that crude opium, or other preparations of it, uneliminated of their thebaine, cannot be tolerated by very many persons who have a very susceptible nervous idiosyncrasy, and this we find also to be the fact in the experience of every physician who is careful enough to note the effects of his medicines. It also explains why the daily use of opium (with this constituent uneliminated), by theriaki or opiophagists, proves so soon a disturber of the general health, and, in the end, so deleterious to the human system. We have a case under observation at the present time, where, ten years ago, the patient was obliged to have recourse to opium to sustain the system against the ravages of pain, but crude opium, laudanum and morphia failing to give relief, McMunn's Elixir as a substitute, had to be resorted to, which proved effective. The long persistence of the case unfortunately ended in the acquirement of a habit unable to be broken, and the person, for

seven years, took McMunn's Elixir in teaspoonful doses three times a day, and for the last three years equivalent doses of dethebainated opium. This he is enabled to do without any increase of the dose, or the least apparent impairment of the constitution. In this case, if preparations of opium not deprived of its thebaine had been used for that length of time, unequivocal signs of the toxicological effects of opium would most certainly have been developed.

If, as has been proved by the experiments and clinical observations of those distinguished physiologists, the three soporific alkaloids in SVAPNIA each have peculiar and specific actions upon the brain and spinal marrow, and located in various and different portions of the same, *it is plainly evident that their combined effects will be modified and rendered milder in their therapeutical operation than either one separately.* Thus morphine, spending its action exclusively upon the brain, always leaves a disagreeable headache and frequently a nauseated stomach, an irritable temper and haggard look that evinces a pathological state of the whole economy. Codeine, exerting its influence principally on the pneumogastric plexus of nerves, calms the system with its anodyne and hypnotic properties without intensifying the concurrent effects of the morphine. Now, again, narceine having peculiar anodyne and somniferous effects, exerting a special influence upon another portion of the nervous system, still adds to the anodyne powers of the other two alkaloids. *Thus the three combined require a less amount of narcotic power than either one alone, and are therefore less liable to produce poisonous effects.* The nauseating and sometimes convulsive effects of opium, in many cases, is equivalent to the poisonous operation of thebaine and the sickening effects of the disagreeable odorous principle, whilst the elimination of those principles from the SVAPNIA is evinced by the absence of those disagreeable symptoms. So active a principle as thebaine taken into the system by the habitual opium-taker for a long time, must necessarily impair and injure the constitution far more than those preparations of opium which do not contain it; and this accords

well with the experience of thousands who have unfortunately acquired the habit of, or necessity for, its daily use.

Dr. Flukeger, of Berlin, without discovering any new principle in opium pure enough to distinguish it, has, in numerous analytical experiments, shown by first infusing powdered opium in benzol so as to extract the principal part of the narcotine and caoutchouc, that the balance yields to alcohol most of the known alkaloids *and about twenty per cent of principles, of the composition and properties of which we yet know nothing.* With so large an amount of *unrecognized* principles, he may well ask "What is Opium?" which is the heading of his article. A long time ago, Dr. Pereira stated that the extractive matter of opium, for the following reasons, must possess much of the powers of opium: 1st. It has been ascertained that after the morphine has been separated from an infusion of opium by magnesia, the filtered liquor gives, by evaporation, an extract which produces the same kind of narcotic effect that opium does. 2d. The effects of the known active principles of opium are not sufficiently powerful to authorize us to refer the whole of the active properties of opium to them. Thus, on an average, one hundred parts of opium yield from eight to ten parts of morphine, and, therefore, if this alkaloid were the only active principle, it ought to be ten or twelve times as powerful as opium is. Now we know that morphine is but little, if at all, more active than opium, and, therefore, the last mentioned substance either contains some other active principle, or the activity of morphine is surprisingly increased by the principle or principles with which it is naturally in combination. Now then, another question arises, equal, we think, in importance to Dr. Flukeger's, and one as yet not answered. Do these unknown principles, soluble in alcohol, possess anodyne and soporific properties? Opianine (or papaverine), partially known, evidently does not. The meconates of morphia and codeia, and the narceia, in whatever combination it may naturally exist in opium, are separable from the other alkaloids and principles without decomposition. Can we not improve upon Dr. Flukeger's plan of analysis by first exhausting the opium of its morphine, codeine and nar-

ceine, and then by means of dilute hydrochloric acid its narcotine, and then the residue with alcohol, and by these means determine some or all of the peculiar principles soluble in this menstruum? Dr. Flukeger candidly admits that he has not yet succeeded in isolating any new principle sufficiently pure to determine its properties. Probably one reason why he has not succeeded better, is that he first dissolves all the matters soluble in alcohol, and these comprise all the active medicinal principles of opium; then with his dozen or more decidedly alkaline bodies, some of them, no doubt, very delicate in their chemical constitution, on the introduction of his reagents to separate those better known, he very probably also alters the combinations of the more delicate and unknown bodies, so that his subsequent reagents have to be modified considerably to detect their presence, or even their existence, much less their distinguishing features. Their affinities in a natural state being broken up, it is not surprising that such delicate bodies require close attention and study to demonstrate their altered condition, and then accurately determine the original state in which they existed in opium. By Dr. Flukeger's plan, he first gets 4.50 narcotine and 6.33 caoutchouc, with traces of fatty matter, by means of benzol. Then 57.67 by alcohol, about 33. of which are the known alkaloids, and the balance mostly unknown principles. Water then extracts 9.67 mucilage, acetic acid 1.73 salts, a little pectic acid and coloring matter. Then ammonia extracts 7.33 pectic acid, reddening litmus. The balance of the one hundred parts consists of cellulose, etc. By extracting the svapnian alkaloids soluble in water first, those which are soluble in alcohol afterwards are so much the more simple, less disturbed by chemical reagents, and consequently more easily investigated.

Prof. Wood says that a good extemporaneous infusion of opium cannot well be made, and then gives the formula of Mr. Eugene Depuy, which can only be preserved by the addition of alcohol. The presence of the spirit is often objectionable, especially where fomentations are needed in otitis, ophthalmias, and the inflammation of other tender organs. To obviate all these difficulties, the following infusion can be made in two minutes, and repeated as often as necessary. R. Svapnia or purified opium, grs. xvi, water

℥ij, mix; or, indeed, it may be made of any strength the necessities of the case may require.

As a topical application in many cases of painful ulcerations, and in all cases where anodyne fomentations are required, it is superior to any infusion of poppy capsules or leaves that can be prepared, and is always at hand.

Comparison of Svapnia with Tinctura Opii Deodorata.

R Svapnia.....	℥ij.
Alcohol.....	℥i.
Water.....	℥ij.

Dissolve the SVAPNIA in the water, and add the alcohol; then filter through paper. Here we have a liquid preparation, equal in every respect to the deodorized tincture of opium, without the circumlocutory difficulties, formalities and expense of preparing that useful medicine. The dose is 15 to 25 drops. It is superior to laudanum or the deodorized tincture in the important respect that it is always of a uniform strength, whereas both of those articles must necessarily vary. Prof. Wood, Dr. Squibb, and all the writers upon this subject, dwell on the extreme variability of the strength of opium, and some of them even go so far as to advise the exclusion of the use of opium, falling back upon the use of morphine instead. In the official formula of the U. S. Pharmacopœia, for the preparation of the deodorized tincture, no provision is made to procure this much needed uniformity. This new official preparation, lately introduced into our national Pharmacopœia, was at first hailed with satisfaction by physicians and apothecaries, as combining, in a liquid form, all the anodyne properties of the drug without the noxious, odorous and resinous principles, and capable of producing its hypnotic effects without subsequent prostration of the nervous system. Want of uniformity in its strength is its greatest drawback.

Comparison of Svapnia with Dr. Squibb's "Liquor Opii Compositus."

Dr. Squibb's preparation has the advantage over the deodorized tincture of opium, of its being made by assay, so that its strength

is always uniform. One fluid ounce contains about 4 grains of morphine, but Dr. S. himself admits that it probably contains very little of the other active matters of the opium. If such be the fact, his preparation has no advantage over morphia.

He has the candor, also, to admit that "in comparison with good powdered opium and laudanum, it seems to be still further behind them in power in proportion to the amount of the drug represented and really present in it. If the powdered opium contains, as it should, 10 per cent of morphine, equal to 12.5 per cent of the sulphate of morphia, then 12.5 drops of the solution should represent one grain of the powdered opium; whilst, in actual practice, nearly double that quantity is required to produce the usual effect in ordinary cases; and in such affections as delirium tremens, in one instance two grains of powdered opium succeeded in procuring sleep after 100 drops of liquor opii comp. had failed." Herein Dr. Squibb's experience exactly tallies with Dr. Pereira with regard to the difference of power between morphine and crude opium. Thus the effects of his preparation practically pretty certainly shows that, after all, it is only a solution of morphia combined with spirit and Hoffman's anodyne. His preparation is even more costly than that of the deodorized tincture, which Mr. Ebert, of Chicago, considers the cause of its not being very generally adopted in the practice of physicians.

Now, SVAPNIA, being much more convenient in form, no considerable advantage, just as uniform in strength, containing all the morphine of the opium, besides, the codeine, which has a decided influence upon the ganglionic system of the upper vertebral column and pneumogastric nerve, and the narceine which spends its force on the lumbar ganglionic system, is equal in every other respect to them. *It will thus be found diffusing its sedative influence over the whole nervous system, instead of being concentrated on the brain, as is done by morphine alone.* The mode of assay adopted in the preparation of Svapnia is somewhat different from that of Dr. Squibb, but the results are exactly the same, producing a *uniformity of strength equal to that of morphine itself.*

With regard to the extractum opii of the shops, Prof. Wood remarks, it is exceedingly doubtful whether anything is left behind

after the opium is exhausted by water, which materially modifies the action of its anodyne principle, and the extract probably has no advantage on this account over opium. Nor has it the advantage of greater uniformity, as the gum extractive, etc., taken up by the water, bear no fixed proportion to the active ingredients.

But, as purely aqueous preparations of opium have been found to agree better with certain individuals, than opium alone or its alcoholic preparations, there is reason to believe that there exists in the crude drug one or more principles capable of causing nausea, headache, nervous disturbance, etc., which are insoluble in water, though extracted by alcohol or ether. M. Guibourt states that this extract, when kept, is apt to swell up, owing, as he at first supposed, to the fermentation of glucose, but he now ascribes the phenomenon to the change of meconic acid into the parameconic, with the escape of carbonic acid.

Dose.—As the relative proportion of the active principles of opium is so very variable, it is hard, if not impossible, to fix a standard for its dose. The difference in constitution, idiosyncrasy, state of the nervous system, and habit, are so various that it is probable there is no other medicine that requires as much care and practical tact in the proper adjustment of the dose as this. Crude opium and laudanum, being the oldest in use, have generally been adopted as a standard.

There are thousands of cases in the practical experience of physicians where a PROPER dose of the anodyne principles of opium may be plainly indicated; and yet the state of the system may, at the same time, be in that critical condition that an overdose may be detrimental, if not fatal. What, then, is the physician to do? His case may be such as to require all the anodyne alkaloids—therefore morphia will not alone meet the indications. Of the officinal preparations, then, he has his choice between crude opium, laudanum, and the deodorized tincture. Now, let him buy his opium himself, and prepare and give the medicine in exact accordance with the directions of the dispensatory; or, if he depends on the apothecary, it is the same; he does not know whether he is giving a quarter dose, a half dose, a full dose, a double dose, or a treble dose, unless the opium or its preparation have either

been analyzed or he has had sufficient experience with that particular sample to learn its strength. If he, by haphazard, gives the quarter dose, he does his patient no good, who may die for the want of the proper dose; if the treble dose, he runs the risk of killing his patient outright by overdosing.

It is to obviate these inherent difficulties, in a great measure, that the new preparation, SVAPNIA, is confidently commended to the favor of the profession.

As the concentration of the strength of so powerful an article of the *Materia Medica* as that of opium is no *desideratum*, I have, in making SVAPNIA, combined with the morphine, codeine and narceine, obtained from opium in a somewhat concentrated form, a material as inert as water, in exact proportion to its anodyne power, so as to make it as near the strength of opium of a 9 per cent morphio-metrical strength as possible. After depriving the opium of its thebaine, narcotine, papavarine, pectin, caoutchouc, vegetable fiber, and the peculiarly disagreeable odorous matter, I submit a small quantity to analysis to determine its proportionate anodyne power. I prefer Dr. Pereira's method to Dr. Squibb's. I then proportion my diluent exactly by arithmetical process, according to the strength of my product, so as to make an exact percentage of anodyne power in my final result. In my report to the State Medical Society upon the subject of New Remedies, I advert to the fact that SVAPNIA is probably nearest allied to the English extractum opii. "By the process I adopt to extract the anodyne principles, I think my preparation possesses more of them than the English article; but, independently of that, I know it is *far more convenient for every form of exhibition*. The English extract varies indefinitely in its strength, according to the opium from which it is prepared, and cannot be kept unless excluded from both heat and the moisture of the open air, whereas SVAPNIA will keep for any time without the least deterioration, and is ready for instant use, either in a solid or liquid form.

Prof. Wood says the dose of the *extract* opium is about one-half of that of opium itself. One grain of SVAPNIA, then, is about equivalent to half a grain of extract, or one-third of a grain of morphia.

VARIOUS FORMULÆ

In which Scapnia, or Bigelow's Purified Opium, replaces Opium to advantage.

Dr. Bigelow's Pectoral, Paregoric Elixir.

Svapnia.....	One hundred and twenty grains.
Benzoic Acid.....	Ninety grains.
Camphor.....	Ninety grains.
Oil of Anise.....	Sixty grains.
Ipecacuanha.....	Ninety grains.
Diluted Alcohol.....	Two pints.

Mix, macerate seven days, and filter through paper. A pleasant anodyne, and antispasmodic, superior to the Official Paregoric, much preferable as an addition to cough mixtures, etc. Dose from one to two fluid drachms, for an adult.

Improved Dovers Powders.

Svapnia, Ipecac: each, in fine powder.....	Sixty grains.
Sulphata Potassa, in fine powder.....	One troy ounce.

Mix by long trituration, in a mortar. Dose, five to fifteen grains.

Solution of Svapnia, representing McMunn's Elixir, and unofficial preparations of that class.

Svapnia.....	One part.
Water.....	Eight parts.
Alcohol.....	Four parts.

Mix and solve. Medium dose, thirty drops.

Powder of Kino and Svapnia.

Kino, in fine powder.....	Three troy ounces and three-quarters.
Svapnia, in fine powder.....	One quarter of a troy ounce.
Cinnamon, in fine powder.....	One troy ounce.

Mix intimately by trituration. An anodyne astringent powder. Twenty grains contain one grain of Svapnia. Dose, five to twenty grains.

Pills of Svapnia Compound.

Svapnia.....	Ten grains.
Camphor, in powder; Extract of Hyoscyamus, of each.....	Twenty grains.

Mix, and make into twenty pills. Dose, two to six. An excellent anodyne in neuralgia, spasmodic affections, rheumatism, gout, hysteria, and various pectoral diseases, as catarrh, whooping cough, asthma, phthisis, etc.

Ointment of Galls and Svapnia.

Nuttall, in fine powder.....	Eighty grains.
Svapnia, in fine powder.....	Thirty-six grains.
Prepared Lard.....	One troy ounce.

Mix well together. This forms an improvement on the Ointment of Galls and Opium of the Pharmacopœia, on account of the solubility of the Svapnia. Acetate of Lead, Camphor, or Tannin, may be added, if deemed necessary.

Wine of Svapnia.

Svapnia.....	One troy ounce.
Sherry Wine.....	Ten fluid ounces.
Comp. Spirits of Lavander.....	Four fluid ounces.

Dissolve the Svapnia in the Wine, and add the Comp. Spirits of Lavander; filter. Dose, fifteen to sixty drops. This is a substitute for the Laudanum of Sydenham, and forms one of the best preparations heretofore devised for use in *delirium tremens*.

SVAPNIA IS SOLD IN BOTTLES OF ONE OUNCE AND HALF OUNCE ONLY. TRIAL PARCELS of the value of 50 cents or \$1, will be furnished upon the receipt of either of these amounts by the manufacturer, and sent (postage paid) by mail to all physicians and others desiring to test the article.

The price per ounce will always be at least *three-fourths less than that of the Sulphate Morphia*, and in case medical men cannot find it in the drug stores of their neighborhood, the manufacturer will send it (postage paid) upon the receipt of price.

The title of Purified Opium, SVAPNIA (from the Sanscrit, signifying sleep), is copyrighted as Trade-Mark.

* * Reference, by permission, is made to Zina Pitcher, M. D., late President National Medical Association; Prof. S. G. Armor, Long Island Medical College; Prof. E. W. Jenks, Detroit Medical College; Prof. H. W. Lyster, University of Michigan; Dr. G. P. Andrews, Editor Detroit Review of Medicine and Pharmacy.

The above preparations manufactured only by

FREDERICK STEARNS, Chemist,
DETROIT, MICHIGAN,

And for sale by Druggists generally in the United States and Dominion of Canada.